

STIC-ILL

From: Marx, Irene
Sent: Tuesday, June 18, 2002 1:33 PM
To: STIC-ILL
Subject: pct 02/10843
Importance: High

NOV 18
400299

Please send to Irene Marx, Art Unit 1651; CM1, Room 10E05, phone 308-2922, Mail box in 11B01

Screening of high-yielding carbamoyltobramycin strains
AU Zhang, Yixuan; Bai, Xiufeng; He, Jianyong; Wang, Minglin
CS Department of Pharmaceutics, Shenyang Pharmaceutical University, Shenyang,
110015, Peop. Rep. China
SO Shenyang Yaoke Daxue Xuebao (1999), 16(1), 53-57

A microbiological technique for determination of tobramycin and apramycin
in a cultural broth of a producer synthesizing a complex of aminoglycoside
antibiotics

AU Sinyagina, O. P.; Zhiganova, L. P.; Lapchinskaya, O. A.;
Lavrova-Balashova, M. F.; Ponomarenko, V. I.
CS Nauchno-Issled. Inst. Izyskaniyu Nov. Antibiot., RAMN, Moscow, 119867,
Russia
SO Biotekhnologiya (1996), (2), 60-64

Aminoglycoside antibiotic 83-1050B. I. Cultural characteristics of
antibiotic 83-1050B-producing strain and its in vitro antimicrobial
activities

AU Han, Yiyun; Mu, Lianjun; Li, Junying; Chen, Xiaoping
CS Sichuan Ind. Inst. Antibiot., Chengdu, Peop. Rep. China
SO Kangshengsu (1986), 11(3), 183-9

SEPARATION OF NEBRAMYCIN COMPONENTS BY THIN LAYER CHROMATOGRAPHY.

AU KADAR-PAUNCZ J
CS RES. INST. PHARM. CHEM., BUDAPEST, HUNG.
SO J CHROMATOGR, (1979) 170 (1), 203-208.
CODEN: JOCRAM. ISSN: 0021-9673.

NEBRAMYCIN SEPARATION OF THE COMPLEX AND IDENTIFICATION OF FACTORS 4 5 AND
5-PRIME.

AU KOCH K F; DAVIS F A; RHOADES J A
SO J. Antibiot., (1973) 26 (12), 745-751.

Irene Marx
Art Unit 1651
CMI 10-E-05,
Mail Box 11-B-01
703-308-2922



=> s carbamoyl tobramycin
 19223 CARBAMOYL
 9 CARBAMOYLS
 19227 CARBAMOYL
 (CARBAMOYL OR CARBAMOYLS)
 3905 TOBRAMYCIN
 5 TOBRAMYCINS
 3907 TOBRAMYCIN
 (TOBRAMYCIN OR TOBRAMYCINS)
 L3 4 CARBAMOYL TOBRAMYCIN
 (CARBAMOYL (W) TOBRAMYCIN)

=> d l3 ab bib tot

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
 AB A tobramycin-producing strain, *Streptomyces tenebrarius* 163, was mutated by magnetic field, magnetic field combined with acridine and resisted by carbamoyltobramycin, carbamoyltobramycin combined with magnetic field. Several high-yielding mutants were selected out. After flask rescreening, these mutants' potency and the content of carbamoyltobramycin increased by > 25% than those of the parent strain.
 AN 1999:194502 CAPLUS
 DN 131:31075
 TI Screening of high-yielding carbamoyltobramycin strains
 AU Zhang, Yixuan; Bai, Xiufeng; He, Jianyong; Wang, Minglin
 CS Department of Pharmaceutics, Shenyang Pharmaceutical University, Shenyang, 110015, Peop. Rep. China
 SO Shenyang Yaoke Daxue Xuebao (1999), 16(1), 53-57
 CODEN: SYDXFF; ISSN: 1006-2858
 PB Shenyang Yaoke Daxue Xuebao Bianjibu
 DT Journal
 LA Chinese

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
 AB A microbiol. method of the differentiated detn. of carbamoyl tobramycin and apramycin in a cultural broth of a producer that forms a nebramycin complex of aminoglycoside antibiotics has been developed. The method is based on the selective sensitivity of an obtained mutant N105 of *Rhizobium meliloti* to carbamoyl tobramycin and tobramycin (up to 50 .mu./mL) and also on nearly complete resistance of the test culture towards apramycin and kanamycin (6000 .mu.g/mL and upper). The 200 times difference in resistance of test microbes *Bacillus subtilis* ATCC 6633 and *Rh. meliloti* N105 to tobramycin and apramycin makes it possible to use a technique of diffusion into agar for monitoring the contents of tobramycin and apramycin during every step of the prodn. of the antibiotics. The relative error of the anal. as detd. in model solns. is equal to 5-10%.
 AN 1997:97359 CAPLUS
 DN 126:168922
 TI A microbiological technique for determination of tobramycin and apramycin in a cultural broth of a producer synthesizing a complex of aminoglycoside antibiotics
 AU Sinyagina, O. P.; Zhiganova, L. P.; Lapchinskaya, O. A.; Lavrova-Balashova, M. F.; Ponomarenko, V. I.
 CS Nauchno-Issled. Inst. Izyskaniyu Nov. Antibiot., RAMN, Moscow, 119867, Russia
 SO Biotekhnologiya (1996), (2), 60-64
 CODEN: BTKNEZ; ISSN: 0234-2758
 PB Biotekhnologicheskaya Akademiya RF
 DT Journal
 LA Russian

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS

AB The sepn. of the nebramycin components by silica gel TLC using a mobile phase of MeOH-EtOH-25% NH3 was studied. The crit. pair apramycin/kanamycin B was successfully resolved. A charring procedure was tested and found suitable for the densitometric in situ quantitation of apramycin, kanamycin B, tobramycin, and **carbamoyle tobramycin** over the range of 2.5-55 .mu.g/per spot.

AN 1990:637915 CAPLUS
 DN 113:237915
 TI Determination of nebramycin components by TLC and densitometry
 AU Eneva, G.; Nikolova-Damyanova, B.; Spassov, S.; Haimova, M.
 CS Inst. Org. Chem., Sofia, 1040, Bulg.
 SO Journal of Planar Chromatography--Modern TLC (1990), 3(May-June), 232-5
 CODEN: JPCTE5; ISSN: 0933-4173
 DT Journal
 LA English

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS

AB Streptomyces tenebrarius Strain 83-1050B produced the antibiotic 83-1050B complex which contained 3 components, including 83-1050B-I and 83-1050B-III. The components 83-1050B-I and 83-1050B-III were identified as apramycin (I) and 6''-O-carbamoyltobramycin (II), resp. Hydrolysis of II formed tobramycin (III). The minimal inhibitory concn. (MIC) of III against Pseudomonas aeruginosa was 1.56 .mu.g/mL, and the MICs of gentamicin, II, antibiotic 83-1050B complex, and I were 12.5, 6.25, 25, and 25 .mu.g/mL, resp. The activities against other bacteria were: III > II = gentamicin > antibiotic 83-1050B complex = I. The antibacterial activity of I and III were reduced by addn. of NaCl in the culture medium. The pH also affected the activities.

AN 1986:511851 CAPLUS
 DN 105:111851
 TI Aminoglycoside antibiotic 83-1050B. I. Cultural characteristics of antibiotic 83-1050B-producing strain and its in vitro antimicrobial activities
 AU Han, Yiyun; Mu, Lianjun; Li, Junying; Chen, Xiaoqing
 CS Sichuan Ind. Inst. Antibiot., Chengdu, Peop. Rep. China
 SO Kangshengsu (1986), 11(3), 183-9
 CODEN: KANGDS; ISSN: 0254-6116
 DT Journal
 LA Chinese

=> DIS HIST

(FILE 'HOME' ENTERED AT 07:55:33 ON 20 DEC 2002)

FILE 'REGISTRY' ENTERED AT 07:55:41 ON 20 DEC 2002

L1 1 S TOBRAMYCIN/CN
 L2 0 S CARBAMOYL TOBRAMYCIN/CN

FILE 'CAPLUS' ENTERED AT 07:57:53 ON 20 DEC 2002

L3 4 S CARBAMOYL TOBRAMYCIN

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Executing the logoff script...

=> d ab bib 1-10

L2 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2002 ACS

AB A tobramycin-producing strain, *Streptomyces tenebrarius* 163, was mutated by magnetic field, magnetic field combined with acridine and resisted by carbamoyltobramycin, carbamoyltobramycin combined with magnetic field. Several high-yielding mutants were selected out. After flask rescreening, these mutants' potency and the content of carbamoyltobramycin increased by > 25% than those of the parent strain.

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SO Shenyang Yaoke Daxue Xuebao (1999), 16(1), 53-57

CODEN: SYDXFF; ISSN: 1006-2858

PB Shenyang Yaoke Daxue Xuebao Bianjibu

DT Journal

LA Chinese

L2 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2002 ACS

AB A microbiol. method of the differentiated detn. of **carbamoyl tobramycin** and apramycin in a cultural broth of a producer that forms a nebramycin complex of aminoglycoside antibiotics has been developed. The method is based on the selective sensitivity of an obtained mutant N105 of *Rhizobium meliloti* to **carbamoyl tobramycin** and **tobramycin** (up to 50 .mu./mL) and also on nearly complete resistance of the test culture towards apramycin and kanamycin (6000 .mu.g/mL and upper). The 200 times difference in resistance of test microbes *Bacillus subtilis* ATCC 6633 and *Rh. meliloti* N105 to tobramycin and apramycin makes it possible to use a technique of diffusion into agar for monitoring the contents of tobramycin and apramycin during every step of the prodn. of the antibiotics. The relative error of the anal. as detd. in model solns. is equal to 5-10%.

AN 1997:97359 CAPLUS

DN 126:168922

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Lavrova-Balashova, M. F.; Ponomarenko, V. I.

CS Nauchno-Issled. Inst. Izyskaniyu Nov. Antibiot., RAMN, Moscow, 119867, Russia

SO Biotekhnologiya (1996), (2), 60-64

CODEN: BTKNEZ; ISSN: 0234-2758

PB Biotekhnologicheskaya Akademiya RF

DT Journal

LA Russian

L2 ANSWER 3 OF 10 WPIDS (C) 2002 THOMSON DERWENT

AB SU 1735368 A UPAB: 19931113

Addn. of cotton-seed flour (I) and sugar beet powder (II) to the fermentation medium used in the prodn. of antibiotic aminoglycoside complex improves its properties. The mixt. contains (in wt.%): soya flour 1.9-2.1, (I) 1.4-1.6, (II) 2.4-2.6, MgSO₄ 1-1.2, NH₄Cl 0.5-0.7, chalk 0.6-0.8, animal fat 1.4-1.6 and water the rest. (I) is a source of C,N,P and microelements. (II) supplies carbohydrates. *Streptomyces cremeus* subsp. *nebramycini* is used as producer strain and it is grown in the medium for 24 hrs. at 37+-1 deg.C with stirring and aeration. The antibiotic complex contains **carbamoyl-tobramycin**, **carbamoyl-kanamycin** and apramycin.

ADVANTAGE - Addn. of (I) and (II) increases the activity of the medium by 25%. Bul. 19/23.5.92

Dwg.0/0

AN 1993-165418 [20] WPIDS
 CR 1993-165416 [20]; 1993-165417 [20]; 1993-165419 [20]
 DNC C1993-073922

TI Nutrient fermentation medium - used in prodn. of antibiotic amino-glycoside complex from streptomyces cremeus strain, with aeration and stirring.

DC B04 D16
 IN KOVALEV, V N; VOSTROKNUTOVA, G N; ZHIGANOVA, L P
 PA (BIOU) BIOTECH RES INST
 CYC 1

PI SU 1735368 A1 19920523 (199320)* 3p
 ADT SU 1735368 A1 SU 1989-4731518 19890816
 PRAI SU 1989-4731518 19890816

L2 ANSWER 4 OF 10 WPIDS (C) 2002 THOMSON DERWENT
 AB SU 1735367 A UPAB: 19931113
 Soya flour (I) and glucose (II) as the C, N, P and carbohydrate sources are incorporated in the nutrient medium for growing Streptomyces cremeus subsp. nebramycin, used as producer of antibiotic aminoglycoside complex. The mixt. contains (in wt.%): (I) 2.4-2.6, (II) 0.9-1.1, chalk 0.4-0.6, animal fat 0.065-0.85 and water the remainder. The obtd. antibiotic complex contains **carbamoyl-tobramycin**, **carbamoyl-kanamycin** and **apramycin**.
 ADVANTAGE - Use of (I) and (II) increases the activity of the medium by 20%. They are also cheaper than maize extract and glycerine, which they replace. Bul. 19/23.5.92

Dwg.0/0

AN 1993-165417 [20] WPIDS
 CR 1993-165416 [20]; 1993-165418 [20]; 1993-165419 [20]
 DNC C1993-073921

TI Nutrient fermentation medium - for prodn. of antibiotic amino-glycoside complex using specified streptomyces cremeus strain as producer.

DC B04 D16
 IN KOVALEV, V N; VOSTROKNUTOVA, G N; ZHIGANOVA, L P
 PA (BIOU) BIOTECH RES INST
 CYC 1

PI SU 1735367 A1 19920523 (199320)* 3p
 ADT SU 1735367 A1 SU 1989-4731518 19890816
 PRAI SU 1989-4731518 19890816

L2 ANSWER 5 OF 10 WPIDS (C) 2002 THOMSON DERWENT
 AB SU 1735366 A UPAB: 19931113
 Streptomyces cremeus subsp. nebramycin is prepd. for use as producent of antibiotic aminoglycoside complex more efficiently as follows. The vegetative material is inoculated into the liquid culture medium for 24 hours with aeration and stirring. Subsequently morphological characteristics, the pH of the medium and dehydrogenase activity of the mycelium are used as indicators in selecting the standard material. The antibiotic complex produced contains **carbamoyl-tobramycin**, **carbamoyl-kanamycin** and **apramycin**.
 USE/ADVANTAGE - In microbiological and medical industries. The amount of antibiotics produced is increased by 30%. Bul. 19/23.5.92

Dwg.0/0

AN 1993-165416 [20] WPIDS
 CR 1993-165417 [20]; 1993-165418 [20]; 1993-165419 [20]
 DNC C1993-073920

TI Prodn. of Streptomyces cremeus strain - for use as producer of antibiotic amino-glycoside complex.

DC B04 D16
 IN KOVAL, V N; VOSTROKNUTOVA, G N; ZHIGANOVA, L P
 PA (BIOU) BIOTECH RES INST
 CYC 1

PI SU 1735366 A1 19920523 (199320)* 3p

ADT SU 1735366 A1 SU 1989-4731518 19890816
PRAI SU 1989-4731518 19890816

- L2 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
AB The sepn. of the nebramycin components by silica gel TLC using a mobile phase of MeOH-EtOH-25% NH₃ was studied. The crit. pair apramycin/kanamycin B was successfully resolved. A charring procedure was tested and found suitable for the densitometric in situ quantitation of apramycin, kanamycin B, **tobramycin**, and **carbamoyl tobramycin** over the range of 2.5-55 .mu.g/per spot.
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DN 113:237915
TI Determination of nebramycin components by TLC and densitometry
AU Eneva, G.; Nikolova-Damyanova, B.; Spassov, S.; Haimova, M.
CS Inst. Org. Chem., Sofia, 1040, Bulg.
SO J. Planar Chromatogr.--Mod. TLC (1990), 3(May-June), 232-5
CODEN: JPCTE5
DT Journal
LA English
- L2 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2002 ACS
AB Streptomyces tenebrarius Strain 83-1050B produced the antibiotic 83-1050B complex which contained 3 components, including 83-1050B-I and 83-1050B-III. The components 83-1050B-I and 83-1050B-III were identified as apramycin (I) and 6''-O-carbamoyltobramycin (II), resp. Hydrolysis of II formed tobramycin (III). The minimal inhibitory concn. (MIC) of III against Pseudomonas aeruginosa was 1.56 .mu.g/mL, and the MICs of gentamicin, II, antibiotic 83-1050B complex, and I were 12.5, 6.25, 25, and 25 .mu.g/mL, resp. The activities against other bacteria were: III > II = gentamicin > antibiotic 83-1050B complex = I. The antibacterial activity of I and III were reduced by addn. of NaCl in the culture medium. The pH also affected the activities.
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DN 105:111851
TI Aminoglycoside antibiotic 83-1050B. I. Cultural characteristics of antibiotic 83-1050B-producing strain and its in vitro antimicrobial activities
AU Han, Yiyun; Mu, Lianjun; Li, Junying; Chen, Xiaoqing
CS Sichuan Ind. Inst. Antibiot., Chengdu, Peop. Rep. China
SO Kangshengsu (1986), 11(3), 183-9
CODEN: KANGDS; ISSN: 0254-6116
DT Journal
LA Chinese
- L2 ANSWER 8 OF 10 WPIDS (C) 2002 THOMSON DERWENT
AB DE 2921022 A UPAB: 19930901
In a new process for the microbiogical prodn. of the nebramycin complex, (a) a strain of Streptomyces tenebrarius which biosynthesises the nebramycin complex is cultivated in a nutrient medium contg. nebramycin 2, nebramycin 5' and/or nebramycin 6 and the individuals forming growing aerial mycelium and spores in the presence of 10-30 mg ml of these antibiotics are isolated; (b) the resulting new resistant strains are cultivated in a submerged aerobic culture in a nutrient medium contg. N- and C- sources, inorganic salts and (opt.) vegetable and/or animal fats at 30-42 degrees C (pref. 35-38 degrees C); and the nebramycin complex or nebramycin 2, nebramycin 4 and nebramycin 5' accumulating in the medium is isolated.
Nebramycin 2 (apramycin) is used in the treatment of diseases of animals and plants (cf. US 3691279, 3853709, 3876767). Nebramycin 6 (tobramycin), produced by hydrolysis of nebramycin 5' (6''-O-carbamoyl-tobramycin), is a broad-spectrum antibiotic used in human medicine, esp. against polyresistant Pseudomonas strains. Use of selected nebramycin-resistant Streptomyces tenebrarius strains allows the prodn. of cultures with high nebramycin concns. thus giving

improved yields.

AN 1979-87983B [49] WPIDS

TI Nebramycin antibiotic complex microbiological prodn. - by cultivation of nebramycin-resistant strains of Streptomyces tenebrarius.

DC B04 D16

IN AMBRUS, G; GYIMESI, J; OTT, I

PA (GYOG) GYOGYSZERKUTATO INTEZET

CYC 4

PI DE 2921022 A 19791129 (197949)*

FR 2426736 A 19800125 (198010)

HU 17756 T 19800228 (198011)

AT 7903572 A 19801214 (198102)

DE 2921022 C 19871015 (198741)

PRAI HU 1978-G1404 19780523

L2 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AB A TLC method was developed for the detection of major nebramycin components, for the separation of tobramycin from other components and for studying the hydrolysis of carbamoyl derivatives and procedures for isolation and purification. A sensitive method was also established for the detection of kanamycin B in tobramycin and for the assay of apramycin in kanamycin B.

AN 1979:230634 BIOSIS

DN BA68:33138

TI SEPARATION OF NEBRAMYCIN COMPONENTS BY THIN LAYER CHROMATOGRAPHY.

AU KADAR-PAUNCZ J

CS RES. INST. PHARM. CHEM., BUDAPEST, HUNG.

SO J CHROMATOGR, (1979) 170 (1), 203-208.

CODEN: JOCRAM. ISSN: 0021-9673.

FS BA; OLD

LA English

L2 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1974:49249 BIOSIS

DN BR10:49249

TI NEBRAMYCIN SEPARATION OF THE COMPLEX AND IDENTIFICATION OF FACTORS 4 5 AND 5-PRIME.

AU KOCH K F; DAVIS F A; RHOADES J A

SO J. Antibiot., (1973) 26 (12), 745-751.

CODEN: JANTAJ. ISSN: 0021-8820.

FS BR; OLD

LA Unavailable

=> DIS HIST

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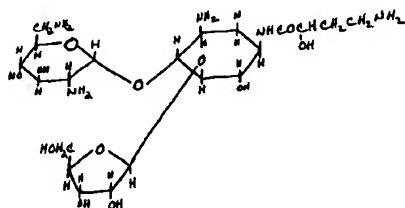
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E CARBAMOYL TOBRAMYCIN/CN
E TOBRAMYCIN/CN

FILE 'CAPLUS, BIOSIS, MEDLINE, USPATFULL, WPIDS' ENTERED AT 13:28:31 ON 18 JUN 2002

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L2 10 DUP REM L1 (1 DUPLICATE REMOVED)

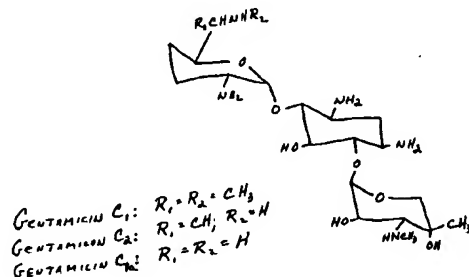
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13.6 Gentamicin or derivative:

This subclass is indented under subclass 4.1.

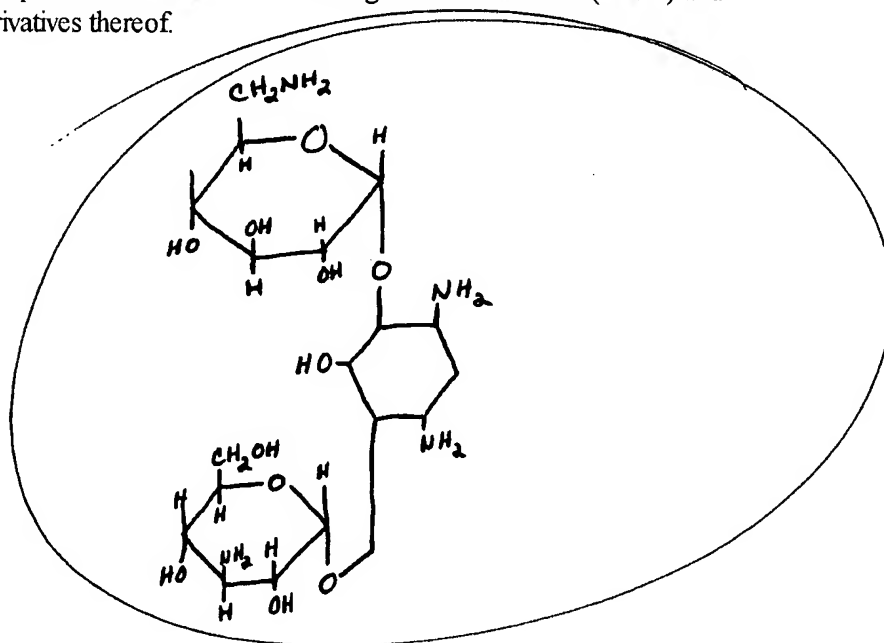
Compounds which have the following structural formula (below) and derivatives thereof.



13.7 Kanamycin or derivative:

This subclass is indented under subclass 4.1.

Compounds which have the following structural formula: (below) and derivatives thereof.



13.8 Carbonyl bonded directly to kanamycin nitrogen:

This subclass is indented under subclass 13.7.

Compounds which include at least one carbonyl group directly bonded to a